



PATENT  
Attorney Docket No. MEE-002

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

APPLICANT(S): Miller *et al.*

SERIAL NO.: 09/780,142

GROUP NO.: 1644

FILED: February 9, 2001

EXAMINER: Huynh, Phuong N.

TITLE *METHODS AND COMPOSITIONS FOR TREATING CONDITIONS OF THE EYE*

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Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

***DECLARATION OF JOAN W. MILLER, M.D., UNDER 37 CFR 1.132***

I, Joan W. Miller, M.D., hereby declare as follows:

1. Since 1991, I have been employed as a member of the full-time faculty of the Massachusetts Eye and Ear Infirmary ("MEEI"). I am currently the Henry-Willard Williams Professor of Ophthalmology at Harvard Medical School, and I am the Chair of the Department of Ophthalmology at Harvard Medical School. I also am the Chief of Ophthalmology at the MEEI. A copy of my curriculum vitae is attached to this declaration.
2. I am a retina surgeon, and I perform research in the field of retinal disease. Over the years, my responsibilities at MEEI have included, among other things, supervising, directing and teaching Research and Clinical Fellows in the field of retinal disease.
3. I am a named co-inventor together with Reem Z. Renno, M.D. and Evangelos S. Gragoudas, M.D. of the subject matter claimed in the above-identified patent application. I understand that the MEEI is owner of this patent application.

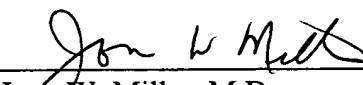
4. I am familiar with the pending patent application, the pending claims, and the outstanding Office Action in which claims 33-35, 39-43, and 47-49 are rejected under 35 U.S.C. §103(a), as unpatentable over U.S. Patent No. 6,270,749 to Blumenkranz *et al.* (“Blumenkranz”) in view of Adamis *et al.* (1996), Arch. Ophthalmol. 114:66-71 (“Adamis”) or U.S. Patent No. 6,342,219 to Thorpe *et al.* (“Thorpe”); claims 33-35, 39-43, and 47-49 are rejected under 35 U.S.C. §103(a), as unpatentable over Kramer *et al.* (1996), Ophthalmology 103(3):427-438 (“Kramer”) in view of U.S. Patent No. 5,733,876 to O’Reilly *et al.* and Adamis or Thorpe; and claims 33-35, 39-43, and 47-49 are rejected under 35 U.S.C. §103(a), as unpatentable over Kramer in view of Blumenkranz and Adamis or Thorpe.
5. I am providing the following information in support of our position that the synergistic result of the combination of photodynamic therapy (“PDT”) with administration of an anti-angiogenesis factor was unexpected.
6. Example 1 of the above-identified patent application indicates that PDT conducted with lutetium texaphyrin (“Lu-TeX”) photosensitizer, a tetrapyrrole derivative, in combination with angiostatin treatment specifically and synergistically kills bovine retinal capillary endothelial (“BRCE”) cells in comparison to retinal pigment epithelium (“RPE”) cells. As shown in Table 1, under the irradiation dose condition of 5 J/cm<sup>2</sup>, PDT using Lu-TeX photosensitizer led to cell survival of 79.13 ± 4.05 percent (mean percent cellular survival ± SD) of the BRCE cells, angiostatin treatment alone led to cell survival of 87.39 ± 5.76 percent of the BRCE cells, and angiostatin treatment followed by PDT using Lu-TeX photosensitizer led to cell survival of 55.22 ± 3.65 percent of the BRCE cells. Thus, the interactive *in vitro* anti-endothelial effect of combined treatment with angiostatin and PDT using Lu-TeX photosensitizer are greater than additive when compared with the sum of expected effects of each treatment alone. This effect appeared to be even more pronounced when the PDT was performed at an irradiation dose condition of 20 J/cm<sup>2</sup>. In this experiment, also as shown in Table 1, PDT using Lu-TeX photosensitizer led to cell survival of 33.34 ± 2.26 percent of the BRCE cells, angiostatin treatment alone led to cell survival of

87.39  $\pm$  5.76 percent of the BRCE cells, and angiostatin treatment followed by PDT using Lu-Tex photosensitizer led to cell survival of 0.90  $\pm$  0.32 percent of the BRCE cells.

7. In contrast, as shown in Table 1 of Example 1, under the irradiation dose condition of 5 J/cm<sup>2</sup>, PDT using Lu-Tex photosensitizer led to cell survival of 94.55  $\pm$  1.60 percent of the RPE cells, angiostatin treatment alone led to cell survival of 99.09  $\pm$  0.8 percent of the RPE cells, and angiostatin treatment followed by PDT using Lu-Tex photosensitizer led to cell survival of 91.84  $\pm$  7.97 percent of the RPE cells. As with the 5 J/cm<sup>2</sup> condition, when PDT was performed at 20 J/cm<sup>2</sup> the effects of PDT and angiostatin on cell viability appeared to be cumulative with one another when combined. Accordingly, no synergistic effect was observed in this cell type under the conditions tested.
8. Accordingly, when PDT was combined with an anti-angiogenesis factor, synergistic cell death was seen in endothelial cells but not in epithelial cells in an *in vitro* system.
9. As mentioned on page 14, lines 1-4 of the patent application, occlusion of the vasculature is a major mechanism of PDT. Occlusion occurs by damage to the endothelial cells, with subsequent platelet adhesion, degranulation, and thrombus formation.
10. However, as mentioned on page 3, lines 10-12 of the patent application, repeated PDT treatments lead to cumulative damage to the RPE cells and choriocapillaris. This may lead to progressive treatment-related vision loss.
11. It was unexpected not only to see a synergistic effect on cell death when combining an anti-angiogenesis factor, such as angiostatin, with PDT using a tetrapyrrole derivative, such as PDT using Lu-Tex photosensitizer, but also to observe this effect only in endothelial cells and not in epithelial cells.
12. Thus, as indicated on page 26, lines 9-10 of the patent application, these results support the potential of combining an anti-angiogenesis factor, such as angiostatin, with PDT using a tetrapyrrole derivative, such as PDT using Lu-Tex photosensitizer, to improve eradication of chroidal neovasculture ("CNV") and to decrease deleterious effects on the RPE.

13. The *in vivo* data presented in an abstract presented in May of 2003 at the Annual Meeting of the Association of Research in Vision and Ophthalmology in Fort Lauderdale, Florida (the "Abstract") (made of record as citation C115) confirm the *in vitro* data presented in Table 1 of Example 1 of the patent application. PDT alone, using verteporfin photosensitizer and an irradiation dose condition of  $10 \text{ J/cm}^2$ , led to a lack of angiographic leakage (i.e., CNV closure) 42.9% of the time at 24 hours and 7 days post-PDT, while PDT under then same conditions in combination with continuous administration of angiostatin initiated before PDT led to lack of angiographic leakage 90% of the time at 24 hours and 100% of the time at 7 days post-PDT. Based on my involvement in these studies, I understand that angiostatin treatment alone had no effect on angiographic leakage and that continuous administration of angiostatin was initiated before PDT in the continuous administration condition. In my opinion, given that angiostatin had no effect, the effect of PDT in combination with angiostatin was greater than the sum of the effects observed with angiostatin alone and PDT alone.
14. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and that such willful false statements may jeopardize the validity of this application or any patent issuing therefrom.

Dated: September 19, 2005

  
Joan W. Miller, M.D.

Date prepared: 9/19/05

**Name:** JOAN WHITTEN MILLER

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243 Charles Street, Boston, MA 02114  
Home Address: 40 Westland Avenue, Winchester, MA 01890  
Email: [jwmiller@meei.harvard.edu](mailto:jwmiller@meei.harvard.edu)  
Telephone: 617-573-3526 Fax: 617-573-3364  
Place of Birth: Toronto, Ontario, Canada  
Canadian citizen; U.S. Permanent Resident

**Education:**

1980 S.B. Massachusetts Institute of Technology, Life Sciences  
1985 M.D. Harvard Medical School, cum laude

**Postdoctoral Training:**

**Internships and Residencies**

1985 - 1986 Intern in Medicine; Newton-Wellesley Hospital, Newton, MA  
1986 - 1989 Ophthalmology Resident; Massachusetts Eye and Ear Infirmary,  
Boston, MA

**Clinical and Research Fellowships**

1989 - 1991 Vitreo-retinal Fellow, Clinical and Research, Retina Service,  
Massachusetts Eye and Ear Infirmary, Boston, MA

**Licensure and Certification:**

1989 Massachusetts Medical License  
1991 American Board of Ophthalmology

**Academic Appointments:**

1986 - 1991 Clinical Fellow, Harvard Medical School  
1991 - 1991 Assistant Professor of Ophthalmology, Tufts University School of  
Medicine  
1991 - 1993 Instructor in Ophthalmology, Harvard Medical School  
1994 - 1997 Assistant Professor of Ophthalmology, Harvard Medical School  
1998 - 2002 Associate Professor of Ophthalmology, Harvard Medical School  
2002 - Professor of Ophthalmology, Harvard Medical School  
2003-2006 Member, Limited Term, Institute of Medical Science, Faculty of  
Medicine, University of Toronto  
2003- Chair, Department of Ophthalmology, Harvard Medical School  
2004- Henry Willard Williams Professor of Ophthalmology Harvard  
Medical School

## Hospital Appointments:

1991 - 1991	Ophthalmologist, New England Medical Center, Boston
1991 - 1996	Assistant Surgeon in Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston
1994-	Courtesy Staff, Mt. Auburn Hospital, Cambridge
1996 - 2002	Associate Surgeon in Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston
1996-	Clinical Associate in Surgery, Massachusetts General Hospital, Boston
1998 -	Consulting Staff in Ophthalmology, Spaulding Rehabilitation Hospital, Boston
2002-	Surgeon in Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston

## Major Administrative Responsibilities

1991	Director, Vitreo-Retinal Service, New England Eye Center, Boston
1991	Assistant Chief of Ophthalmology for Clinical Services, New England Medical Center, Boston
1991 -	Co-Director, Laser Research laboratory, Massachusetts Eye and Ear Infirmary, Boston
1991 -	Pharmacy Committee; Eye Subcommittee Co-Chairman, Massachusetts Eye and Ear Infirmary, Boston
1992 -	Member, Residency Selection Committee, Massachusetts Eye and Ear Infirmary, Boston
1993 - 2003	Co-Chair Continuing Medical Education, Massachusetts Eye and Ear Infirmary, Boston
1996 - 1999	Co-Director Methuen Satellite, Massachusetts Eye and Ear Infirmary, Boston
1998 - 2000	Member, Executive Committee, Massachusetts Eye and Ear Infirmary, Boston
1998 - 2000	Member, Medical Board, Massachusetts Eye and Ear Infirmary, Boston
1998 - 2000	President of the Eye Staff, Massachusetts Eye and Ear Infirmary, Boston
1998 - 1999	President-elect of the Medical Staff, Massachusetts Eye and Ear Infirmary, Boston
1999 - 2000	President of the Medical Staff, Massachusetts Eye and Ear Infirmary, Boston
2000 - 2002	Co-Director, Angiogenesis Laboratory, Retina Research Institute, Massachusetts Eye and Ear Infirmary, Boston
2002-	Director, Angiogenesis Laboratory, Retina Research Institute, Massachusetts Eye and Ear Infirmary, Boston
2003-	Chief of Ophthalmology, Massachusetts Eye and Ear Infirmary
2003-	Member, Board of Directors, Massachusetts Eye and Ear Infirmary
2003-	Member, Board of Directors, Foundation of the Massachusetts Eye and Ear Infirmary, Inc.

2003-	Member, Board of Directors, Massachusetts Eye and Ear Associates, Inc.
2003-	Member, Board of Directors, Massachusetts Eye and Ear Infirmary & Physician Staff, Inc.
2003-	Member, Office of the President, Foundation of the Massachusetts Eye and Ear Infirmary, Inc.
2003-	Member and Chairman, Board of Surgeons, Ophthalmology, Massachusetts Eye and Ear Infirmary
2003-	Member, Budget and Finance Committee, Massachusetts Eye and Ear Infirmary
2003-	Member, Accreditation Committee, Massachusetts Eye and Ear Infirmary
2003-	Member, Patient Care Assessment Committee, Massachusetts Eye and Ear Infirmary
2003-	Member, Conflicts of Interest and Commitment Committee, Massachusetts Eye and Ear Infirmary
2003-	Member, Research Committee, Massachusetts Eye and Ear Infirmary
2003-	Member, Medical Board (medical executive committee), Massachusetts Eye and Ear Infirmary
2003-	Member, Budget and Finance Committee, Massachusetts Eye and Ear Associates, Inc.
2003-	Member, Executive Committee, Foundation of the Massachusetts Eye and Ear Infirmary, Inc.
2003-	Member, Budget and Finance Committee, Foundation of the Massachusetts Eye and Ear Infirmary, Inc.
2003-	Member, Nominating Committee, Foundation of the Massachusetts Eye and Ear Infirmary, Inc.
2003-	Member, Compliance Committee, Foundation of the Massachusetts Eye and Ear Infirmary, Inc.
2003-	Member and Chairman, Department Executive Committee Member Ethics Committee for Patient Care
2003-	Co-Director Retina Research Institute

## Major Committee Assignments

### Massachusetts Eye and Ear Infirmary

1991 - 1992	JCAHO Work Group
1991 - 2001	Pharmacy Committee; Eye Subcommittee Co-Chairman
1992 -	Residency Selection Committee
1993 - 1996	Representative to Mass. General Hospital Clinical Practice Group
1993 -	Co-Chair Continuing Medical Education
1998 - 2000	Member, Medical Board
2001-	Member, Patent Committee
2002- 2003	Member, Executive Research Committee

## Harvard Medical School

1991 - 1995	Harvard Medical Laser Center Board
1993 -	Continuing Medical Education Committee
1996 -1998;	Faculty Search Committee, Department of Ophthalmology,
1999 - 2000	
1998 - 2001	Joint Governance Committee, Center for Clinical Research, Department of Ophthalmology
1998 - 2000	Chairman Joint Governance Committee, Center for Clinical Research Department of Ophthalmology
2002 -	Executive Committee of the Department of Ophthalmology
2003-	Fellowship Review Committee
2003-	Member, Promotions and Reappointments Committee
2003-	Chairman, Executive Committee of the Department of Ophthalmology
2005-	Medical Education Reform Committee
2005-	Co-Chair, Curriculum Design Group on Advanced Clinical and Science Experiences
2005-	Subcommittee of Professors
2005-	Medical Education Reform Committee

## National and Regional

1995 - 2001	Study Advisory Group, Therapy of AMD with Photodynamic Therapy Study Group
	Supervise study, report and write results
2000 - 2003	Scientific Advisory Board for EyeTech Pharmaceuticals
	Supervise preclinical and clinical studies
2002-	American Academy of Ophthalmology Preferred Practice Patterns Retina Panel
2002-	US Pharmacopeia, Expert Committee Reviewer
2002-	American Academy of Ophthalmology Subspecialty Day Committee
2004-	Advisory Board, Women's Eye Health Task Force
2005-	Scientific Advisory Board, Bausch and Lomb

## Memberships, Offices and Committee Assignments in Professional Societies:

1976 - 1980	Delta Psi Social Fraternity, President 1979
1980 - 1985	Tech Alumni Rowing Association
1980 - 1985	Lawrence B. Henderson Society, Harvard Medical School
1984 -	Massachusetts Medical Society
1985 -	Harvard Medical Alumni Association
1987 -	American Medical Association
1989 -	Massachusetts Eye and Ear Infirmary Alumni Association
1992 - 1996	American Diabetes Association
1992 -	American Academy of Ophthalmology
1992 -	American Association for the Advancement of Science
1993 -	Founder, Women's Alumnae, Massachusetts Eye and Ear



	Infirmery, Boston
1993-	Research to Prevent Blindness
1994 -	New England Ophthalmological Society
1995 -	Retina Society
1995-	Macula Society
1996 -	Retina Society Travel Fellowship Committee
1998 -	Club Jules Gonin
1999- 2003	Management Committee, Friends of MIT Crew
1999 -2003	Macula Society, Awards Committee
2003-	Chairman, Macula Society Research Committee
2003-	Macula Society, Executive Committee
2004-	Massachusetts Society of Eye Physicians and Surgeons
2004-	Association of University Professors of Ophthalmology
2004-	Advisory Board, The Women's Eye Health Task Force
2005-	American Society of Retinal Physicians

### Editorial Boards

1998 -	Editorial Board, Eyenet Magazine, American Academy of Ophthalmology
2000-	Guest Editorial Board Member, Investigative Ophthalmology and Visual Science
2003-	Editorial Board, Graefes Archives of Clinical and Experimental Ophthalmology
2004-	Editorial Advisory and Review Board, Retinal Physician
2004	Editorial Board, Archives of Ophthalmology

### Journal Manuscript Review

1992 - 1994	American Ophthalmological Society
1992 -	Ophthalmology
1993 -	Investigative Ophthalmology and Vision Research
1994 -	Current Eye Research
1994 -	Microvascular Research
1994 -	Archives of Ophthalmology
1995 -	Proceedings of the National Academy of Sciences
1996 -	Experimental Eye Research
1996	Reader of a Senior Thesis for Harvard-MIT Division of Health Science and Technology
1996 -	American Journal of Ophthalmology
1997 -	American Journal of Pathology
1997 -	Retina
1997 -	British Journal of Ophthalmology
1998 -	Journal of Cellular Physiology
1998 -	Nature Medicine
1999 -	Diabetes/Metabolism Research and Review
2001-	European Journal of Ophthalmology
2002	Human Gene Therapy

2002-	Canadian Journal of Ophthalmology
2002-	The FASEB Journal
2003-	Molecular Therapy
2004-	New England Journal of Medicine

### **Awards and Honors**

1976	Governor General's Medal, Canada
1980	Phi Beta Kappa
1985	Doctoral Convocation - cum laude
1985	Hewlett Packard Award
1986	Department of Surgery Award, Newton-Wellesley Hospital
1993	American Diabetes Association Research Award
1997	Research to Prevent Blindness Manpower Award
1999	Rosenthal Award from the Macula Society
2000	Macula Society Research Fund
2000	Foundation Fighting Blindness Individual Research Award
2000	Elizabeth S. O'Brien Trust Award
2000	Research to Prevent Blindness Physician-Scientist Award
2000	Popular Science "Best of What's New" Award for Visudyne (see patents)
2000	Business Week "Top Products of 2000" Award for Visudyne (see patents)
2002	Jules Gonin Lecture, Retina Research Award, Club Jules Gonin for Photodynamic Therapy
2002	Alcon Research Institute Award
2003	American Academy of Ophthalmology Achievement Award
2004	John Milton McLean Medal, Weill Medical College of Cornell University
2004	Nominee, 2003-04 Excellence in Mentoring Award, HMS
2004	Nominee, Dean's Award for Leadership in the Advancement of Women Faculty, HMS
2006	ARVO/Pfizer Award, Association for Research in Vision and Ophthalmology

### **Research, Teaching, and Clinical Contributions**

#### **Major Research Interests:**

1. The role of growth factors in ocular neovascularization
2. Pharmacological therapy of intraocular neovascularization, (iris, retina, and choroid)
3. Photodynamic therapy of intraocular neovascularization (iris, retina, and choroid)
4. Local drug delivery to the retina and choroid

Research is directed at the development of new therapies for neovascular diseases of the retina and choroid, particularly age-related macular degeneration and diabetic retinopathy. One strategy has been the development of photodynamic therapy for choroidal neovascularization, from animal studies to clinical trials. This therapy received approval from health authorities in the U.S.

and abroad for the treatment of neovascular macular degeneration and other forms of choroidal neovascularization. Studies are ongoing to improve the selectivity of this therapy, in order to improve vision results and decrease the need for retreatment. A second strategy has been to study the control of pathologic neovascularization, particularly the role of growth factors in retinal and choroidal neovascularization. Vascular endothelial growth factor, (VEGF) was identified as a key factor, and drugs targeting VEGF have been tested in animal models and are in early clinical trials. Finally, new approaches to localized drug delivery to the retina and choroidal are being investigated using a trans-scleral controlled-release approach.

#### Research Funding information:

##### Past

1991 - 1992	Dept. of Ophthalmology PI
1992 - 1993	Experimental Neovascularization DOE (Center for Excellence Grant) PI Photodynamic Therapy of Experimental Choroidal Neovascularization
1992 - 1994	F. Hoffman-La Roche Ltd Co-PI Pharmacological Treatment of Macular Degeneration Study
1992 - 1993	Massachusetts Lions Research Fund Co-PI Hypoxia-Mediated Release of Vascular Endothelial Growth Factor from the Retina
1992 - 1994	F. Hoffman-La Roche Ltd PI Alpha-interferon treatment of iris Neovascularization
1994 - 1995	F. Hoffman-La Roche PI Pharmacological Treatment of Macular Degeneration Study
1993 - 1995	American Diabetes Association PI Application of a Model of Intraocular Neovascularization
1994 - 1995	Massachusetts Lions Eye Research Fund Co-PI Angiography of Experimental Ocular Neovascularization
1993 - 1996	Massachusetts Eye and Ear Foundation PI Experimental Intraocular Neovascularization
1993 - 1996	Quadra-Logic Technologies, Inc. PI Photodynamic Therapy of Experimental Choroidal Neovascularization
1995 - 1996	Quadra-Logic Technologies, Inc. PI Phase I/II Study of Photodynamic Therapy of Choroidal Neovascularization
1995 - 1999	National Cancer Institute Co-investigator Proton Beam Irradiation of Choroidal Melanoma
1996 - 1997	Massachusetts Lions Eye Research Fund PI Photodynamic Therapy of Ocular Neovascularization
1996 - 1997	Genentech, Inc. PI Preclinical evaluation of anti-VEGF agents
1997 - 1998	Massachusetts Lions Eye Research Fund PI Photodynamic Therapy of Ocular Neovascularization

1996 - 1998	Hybridon, Inc. PI
	Evaluation of VEGF antisense oligonucleotides
1996 - 1999	QLT Phototherapeutics/CIBA Vision PI
	Phase III Trial of Photodynamic Therapy for Macular Degeneration
1997 - 1998	Research to Prevent Blindness PI
	Manpower Award
1998 - 1999	Massachusetts Lions Eye Research Fund PI
	Digital fundus angiography
1998 - 1999	Monsanto-Searle Co-PI
	Integrin inhibitors in preclinical models of choroidal Neovascularization
1998 - 2000	Photogen, Inc. PI
	Preclinical evaluation of two-photon PDT
1998- 2001	Photoelectron Corp Co-PI
	Evaluation of photoelectron device for experimental choroidal Neovascularization
1998 - 2000	Agouron Pharmaceuticals Co-PI
	Phase I/II Study of Matrix metalloproteinase inhibitor For AMD
1998 - 2000	QLT Phototherapeutics/CIBA Vision PI
	Verteporfin in Photodynamic Therapy
1999 - 2001	Alcon Laboratories
	Phase I and II Study of Lu-Tex PDT for AMD
1999 - 2000	Macula Society Research Award
	Cellular Mechanisms following PDT
1999 - 2000	Massachusetts Lions Eye Research Fund PI
	Photodynamic therapy
1999 - 2000	Macula Foundation PI
	Evaluation of Angiostatin in Retinal Ischemia Model
1999 - 2000	Alcon Laboratory PI
	Phase I and II Study of Angiostatic Steroid for AMD
1999 - 2000	Genentech, Inc. PI
	Evaluation of VEGF Inhibition in Experimental Choroidal Neovascularization
1999 - 2001	Genentech, Inc. PI
	Phase I and II Study of anti-VEGF Antibody Fragment for AMD
2000	Lions Club International Foundation PI
	Diabetic Retinopathy Studies
1998 - 2001	Alcon Laboratories PI
	Evaluation of Lutetium Texafrin Photodynamic Therapy for Experimental Choroidal Neovascularization
2000 - 2001	Massachusetts Lions Eye Research Fund PI
	Photodynamic Therapy
2000 - 2001	Massachusetts Lions Eye Research Fund PI
	Photodynamic Therapy
2000 - 2002	Genentech, Inc. PI

	Evaluation of VEGF Inhibition and Verteporfin PDT in Experimental Choroidal Neovascularization
2000 - 2002	Allergan, Inc. PI
	Preclinical evaluation of Tyrosine Kinase Inhibitor
2000 - 2002	Research to Prevent Blindness Physician Scientist Award PI
	Apoptosis Research
2001 - 2002	Massachusetts Lions Eye Research Fund PI
	Photodynamic Therapy
2000 - 2003	QLT Phototherapeutics/CIBA Vision PI
	Continuation studies of Verteporfin PDT
2000 - 2003	Elizabeth S. O'Brien Trust PI
	Photodynamic Therapy
2000 - 2003	Foundation Fighting Blindness PI
	Photodynamic Therapy
2000 - 2003	Eyetechnics Pharmaceuticals Co-investigator
	Unrestricted grant for angiogenesis research
2000 - 2003	Iacocca Foundation Co-PI
	Angiogenesis research
2002- 2003	Massachusetts Lions Eye Research Fund PI
	Photodynamic Therapy

## Current

1995 -	Retinal Neovascularization Fund (Philanthropy) PI
2001 - 2006	National Eye Institute; Co-Investigator
	Non-Invasive Measurements of RPE Lipofuscin
2002 -	Visioncare; Co-Investigator
	Phase II and III study of intraocular telescope for AMD
2003-2008	National Eye Institute; Co-Investigator
	Sib-pair study in AMD
2004-2005	Joint Clinical Research Center; Co-Investigator
	PEDF in Retinal Detachment-Apoptosis
2004-	Joint Clinical Research Center; Co-Investigator
	The role of Cathepsin B in Choroidal Angiogenesis
2004-2005	John & Edith Fitzpatrick Fund, MEEI Foundation; Co-investigator
	Evaluation of subretinal fluid following primary macula detachment by optical coherence tomography

## Report of Teaching

Teaching through patient care and discussion of cases with medical students, residents in ophthalmology and clinical fellows takes place during clinics, outpatient lasers and other procedures, and surgery. Seven residents in ophthalmology are trained yearly, and participate in the Retina Service in all three years, including scleral buckling surgery for retinal detachment. Three fellows in medical and surgical retina are trained yearly, and participate in all aspects of patient care. Lectures

and presentations are made at Ophthalmology Grand Rounds and weekly conferences, attended by residents, fellows, and faculty.

Research trainees include 1-2 pre-residency fellows and 3-6 post-doctoral fellows yearly. Weekly meetings of research trainees review ongoing projects and current topics relevant to the research interests of the laboratory. Presentations are prepared and given at local, regional, national and international venues, particularly in the field of macular degeneration and new therapies for neovascular eye disease.

## Local Contributions

### Massachusetts Eye and Ear Infirmary

1986 -	Ophthalmology Grand Rounds, Quarterly presentations 24 residents; 8-20 fellows; 30-50 staff physicians, 1 hour/year (Speaker);
1989 - 1992	Chief's Rounds, Quarterly Presentations 24 residents, 30 fellows, 2 staff physicians 1 hour/year Speaker
1990 - 1992	MEEI Alumni Meeting: Pharmacologic and Photodynamic Modulation of Experimental Iris Neovascularization 100 residents, fellows, staff physicians 10 minutes Speaker
1991 -	Retina Service Staff Outpatient Clinic, Consult Service, Surgery 0-2 medical students, 1 resident, 1-2 fellows 12 months/year
1991	Continuing Medical Education Series: Advances in Ocular Drug Therapy 10 residents, 30 fellows, 15 staff physicians 20 hours (Course Co-director), 20 minutes (Speaker)
1991 -	Retina Service Conference 24 residents; 8 fellows; 10 staff physicians 2 hours/year (Speaker)
1992	Continuing Medical Education Series: Phacoemulsification and Small Incision Cataract Implant Surgery 24 residents, 8-10 fellows; 50 staff physicians, 10 minutes (Speaker)
1992	Continuing Medical Education Series: Ophthalmology for Primary Care: Diabetic Retinopathy and Retinal Manifestations of AIDS 10 residents, 60-70 staff physicians 20 minutes, (Speaker) 20 hours (Course Co-director)
1993	MEEI Alumni Meeting: Clinical Trial of Alpha-interferon for AMD; 100 residents, fellows, staff physicians 10 minutes (Speaker)
1994	Continuing Medical Education Series: Ophthalmology for Primary Care: Diabetic Retinopathy and Retinal Manifestations of AIDS 10 residents, 60-70 staff physicians,

20 minutes (Speaker), 20 hours (Course Co-director)

1994 Continuing Medical Education Series: Phacoemulsification and Small Incision Cataract Implant Surgery  
24 residents, 8-10 fellows; 50 staff physicians  
10 minutes (Speaker)

1994 MEEI Alumni Meeting: The Role of VEGF in Ocular Neovascularization  
100 residents, fellows, staff physicians  
10 minutes (Speaker)

1994 Continuing Medical Education Series: Ophthalmology for Primary Care: Age-related macular degeneration  
10 residents, 60-70 staff physicians,  
20 minutes (Speaker) 20 hours (Course Co-director)

1995 Fifth Annual Claes H. Dohlman Course: Concepts and Controversies in Outcomes Analysis and Clinical Decision Making in Ophthalmology  
8-10 residents, 30 fellows, 15 staff physicians,  
10 hours (Course Co-director)

1995 Continuing Medical Education Series: Ophthalmology for Primary Care: Age-related macular degeneration  
10 residents, 60-70 staff physicians,  
20 minutes (Speaker) 20 hours (Co-director)

1995 Department of Nursing Retina Workshop for Nurses and Technicians: Age-Related Macular Degeneration: Contemporary Manifestations and Treatment  
30-40 nurses,  
10 minutes (Speaker)

1996 Review Course for Residents and Fellows: Acquired Macular Diseases  
20 residents  
1 hour (Speaker)

1997 American Society of Ophthalmic Registered Nurses: Macular Degeneration Update  
30-40 nurses  
30 minutes (Speaker)

1999 Massachusetts General Physicians Organization, AMIL Study Group: Macular Degeneration  
10 physicians  
20 minutes (Speaker)

2000 Continuing Medical Education Series: New Treatments for Neovascular Macular Degeneration, Massachusetts Eye and Ear Infirmary, Boston  
60 physicians  
2 hours (Speaker) 40 hours Course Director.

2001 National Eye Institute Postdoctoral Training Program in the Molecular Basis of Eye Disease, Schepens Eye Research Institute and Massachusetts Eye and Ear Infirmary  
12 postdoctoral students

2002	1 hour (Lecturer) Boston Retina Fellows Program Selected Cases in Macular Disease 12 physicians 1 hour (Speaker)
2002	Pasteur Program for Clinical Scholars Translational Research. The Development of PDT for Macular Degeneration. 15 medical students, 12 research fellows 1 hour (Lecturer)
2004	Pasteur Program for Clinical Scholars Treatment for Neovascular Macular Degeneration 15 medical students, 12 research fellows 1 hour (Lecturer)
2004	Annual and Alumni Meeting Harvard Medical School Department of Ophthalmology: Mariana Mead Lecture 1 hour (Lecturer)
2004	Review Course for Resident and Fellows: Therapeutic Approaches to Retinal Diseases 1 hour

### Leadership Roles, Department of Ophthalmology, Harvard Medical School

1992 - 2003	Co-Director, Continuing Medical Education Series, Department of Ophthalmology, Harvard Medical School Organize program, select and recruit speakers, edit syllabus
1995-	Director Weekly Laboratory and Journal Review Meeting for Laser/Angiogenesis Research Laboratory, Massachusetts Eye and Ear Infirmary
2000	Co-Director, New Treatments for Macular Degeneration, Department of Ophthalmology, Harvard Medical School Organize program, select and recruit speakers, edit syllabus
2003 -	Grand Rounds, ongoing lectures, select and recruit visiting lecturers
2004	Co-Director, Fellows Course, Controversies in Ophthalmology
2004	Co-Director, Annual/ Alumni Meeting, Update on Ophthalmology
2004 -	Grand Rounds, ongoing lectures, select and recruit visiting lecturers
2005	Co-Director, Fellows Course, Ocular Oncology
2005	Co-Director, Residents Course, Ocular Inflammation
2005	Co-Director, HMS Department of Ophthalmology Intensive Cataract Surgical Training Course
2005	Co-Director, Annual/ Alumni Meeting, Update on Ophthalmology
2005 -	Grand Rounds, ongoing lectures, select and recruit visiting lecturers
2005	Co-Coordinator, 8 <sup>th</sup> Annual Harvard Lecture in Ophthalmology, Massachusetts Eye and Ear Infirmary

### Selected Advisees/Trainees



David Guyer, MD	Research and clinical fellow, 1990 – 1992, Chairman, Department of Ophthalmology, New York University School of Medicine, New York, NY
Arthur Walsh, MD	Research and clinical fellow, 1991 – 1993, Private practice, Lebanon, NH
Michal Kramer, MD	Research fellow, 1992 – 1994, Assistant Professor, Department Of Ophthalmology, Rabin Medical Center, Petah Tiqva, Israel
Robert Haimovici, MD	Research and clinical fellow, 1992 – 1994, Assistant Professor of Ophthalmology, Boston University School of Medicine, Boston, MA
Thomas Ciulla, MD	Resident in Ophthalmology, 1992 – 1995, Assistant Professor of Ophthalmology, Indiana University School of Medicine, Indianapolis, IN
Marie-Therese Bernal, MD	Research fellow, 1993 – 1994, Private practice, Bogota, Columbia
William Stinson, MD	Research and clinical fellow, 1994 – 1996, Private practice, Beverly, MA
Deeba Husain, MD	Research fellow 1994 – 1996; 1997 – 1998, Vitreoretinal Fellow, 2001-2003 Assistant Professor of Ophthalmology, Boston University School of Medicine, Boston, MA
Ekaterina Karatza, MD	Research fellow, 1994 – 1996, Resident in Ophthalmology, Louisiana State University Medical Center, Shreveport, LA
Chandler Samiy, MD	Research and clinical fellow, 1994 – 1996, Private practice, Ocala, FL
Michael Tolentino, MD	Research fellow and Resident in Ophthalmology, 1994 – 1999, Assistant Professor of Ophthalmology, Scheie Eye Institute, Philadelphia, PA
Martin Reinke, MD	Research and clinical fellow, 1995 – 1997, Private practice, Dallas, TX
Christina Canakis, MD	Research fellow, 1995 – 1997, Resident in Ophthalmology, University of Athens, Athens, Greece
James Palmer, MD	Research and clinical fellow, 1996 – 1998, Private Practice Mountain View, CA
Robert Bhisitkul, MD, PhD	Research and clinical fellow, 1996 – 1998, Assistant Professor of Ophthalmology, University of California San Francisco, San Francisco, CA
Panos G. Theodossiadis, MD	Research fellow, 1996 – 1998, Assistant Professor of Ophthalmology, University of Athens Medical School, Athens, Greece
Jean Daniel Arbour, MD	Research and clinical fellow, 1997 – 1999, Assistant Professor of Ophthalmology, University of Montreal, Montreal, Canada

Timothy You, MD	Research and clinical fellow, 1997 – 1999, Private practice, Eugene, OR
Evandro Lucena, MD	Research fellow, 1997 – 1999, Private practice, Rio de Janeiro, Brazil
Sam Razavi, MD	Research fellow, 1998 – 1999, Retina fellow, University of Creteil, Creteil, France
Kenneth Graham, MD	Research and clinical fellow, 1998 – 2000, Clinical Instructor, University of Maryland, Baltimore, MD
Magda Krzystolik, MD	Research and clinical fellow, 1998 – 2000, Assistant Clinical Professor, Brown University, Providence, RI
Rosa Y. Kim, MD	Research and clinical fellow, 1998 – 2000, Private practice, Houston, TX
Hogara Taguchi, MD	Research fellow, 1998 – 2000, Assistant Professor of Ophthalmology, Kyoto University, Japan
Jay Ambati, MD	Research and clinical fellow, 1998-2001 Assistant Professor of Ophthalmology, University of Kentucky, Lexington, KY
Danny Gauthier, MD	Research and clinical fellow, 1999-2001 Assistant Professor of Ophthalmology, University of Montreal, Montreal, Canada
Ron Afshari, MD	Research and clinical fellow, 1999-2001 Assistant Professor of Ophthalmology, Yale University School of Medicine, New Haven, CT
Eric Ezra, MD	Research Fellow, 2000-2001 Surgeon, Moorfields Eye Hospital, London, England
Eugene Lit, MD	Research and clinical fellow, 2000-2002 Assistant Clinical Professor of Ophthalmology, University of California, San Francisco, CA
Ayman Youssri, MD	Research and clinical fellow, 1999-2002 Assistant Professor of Ophthalmology, University of Cairo, Cairo, Egypt
David N. Zacks, MD PhD	Research and clinical fellow, 2002-2002 Assistant Professor of Ophthalmology, University of Michigan, Ann Arbor, Michigan
Reem Z. Renno, MD	Research fellow, 1998-2002 Resident in Ophthalmology, University of California Los Angeles, Los Angeles, CA
Yoshiko Terada, MD	Research fellow, 2000-2002 Assistant Professor of Ophthalmology, Okayama University, Okayama, Japan
Karen Carasquillo, PhD	Post-doctoral fellow, 2000-2002 Massachusetts School of Optometry, Boston, MA
Ivana Kim, MD	Resident 1998-2001, Research and clinical fellow, 2001-2003 Instructor in Ophthalmology, Mass. Eye and Ear Infirmary, Harvard Medical School

Subranhsu Ray, MD PhD	Resident 1997-2000, Chief Resident 2000-2001; Research and clinical fellow, 2001-2003 Private Practice, San Francisco, CA
Tara Young, MD	Research and clinical fellow, 2002-2004 Assistant Professor of Ophthalmology, University of California, Los Angeles, CA
Atul Sharma, MD	Research and clinical fellow, 2002-2004 Private Practice
John Christophoridis, MD	Research and clinical fellow, 2003-2005 Instructor in Ophthalmology, Beth Israel Deaconess Medical Center, Boston, MA
Lucia Sobrin, MD	Research and clinical fellow, 2003-2005 Clinical fellowship, Immunology/Uveitis
Jennifer Sun, MD	Research and clinical fellow, 2003-2005 Instructor in Ophthalmology, Joslin Diabetes Center; participant, HMS Clinician-Scientist Mentorship Program

## Regional, National, and International Contributions

### Presentations

1987	Greater Boston Lecture Series: The Retinal Manifestations of AIDS (Speaker)
1991	Third International Congress on Laser Technology in Ophthalmology: Phthalocyanine Photodynamic Therapy of Iris Neovascularization (Speaker)
1991 - 1992	Retina Society: Systemic Alpha-Interferon for Intraocular Neovascularization (Speaker)
1991	Laser Therapy of Ocular Disease (Speaker and Course Co-Director)
1991	Greater Boston Lecture Series; Retina Section (Speaker and Course Co-Director)
1992	Invited Speaker, Rhode Island Ophthalmological Society: Pharmacologic Therapy of Intraocular Neovascularization
1992	Invited Speaker, Lahey Clinical Ophthalmology Grand Rounds: Pharmacologic Therapy of Intraocular Neovascularization
1993	ARVO: AGM - 1470 Treatment of Experimental Intraocular Neovascularization (Speaker)
1993	Invited Speaker, MGH Laser Center Symposia: Photodynamic Therapy in Ophthalmology
1993	Retina Society: VPF/VEGF Levels in Experimental Neovascularization (Speaker)
1993	Invited Speaker, Walter Wright Day, University of Toronto: Posterior Segment Complications of Cataract Surgery
1994	Invited Speaker, Update on Retinal Diseases for the Anterior Segment Surgeon, Newport, RI: Update on Background Diabetic Retinopathy: New approaches to the treatment of Macular Degeneration

- 1994 Club Jules Gonin, Versailles, France: VEGF Levels in Experimental and Clinical Neovascularization (Speaker)
- 1994 Retina Society, Williamsburg, VA: Photodynamic Therapy of Experimental CNV Using Liposomal Benzoporphyrin Derivative (Speaker)
- 1994 Invited Speaker, Endocrine Conference, Massachusetts General Hospital: Diabetic Retinopathy
- 1995 ARVO: Inhibition of VEGF Prevents Ocular Neovascularization in a Monkey Model (Speaker)
- 1995 Invited Speaker, New England Chapter Ophthalmic Photographers Society: Alternative Dyes for Digital Angiography
- 1995 Invited Speaker, Schepens Eye Research Institute, Boston, MA: The Role of VEGF in a Model of Ocular Neovascularization
- 1995 Invited Speaker, Hale Hospital, Haverhill, MA: Aging and Vision Loss
- 1995 Kevin Hill Ophthalmology Course. Update on Retinal Disease. Neovascular Disorders and Pediatric Retina. (Course Director and Speaker)
- 1995 Invited Speaker, Longwood Medical Area (Brigham and Women's Hospital), Boston, MA: New Treatments for Macular Degeneration
- 1995 Retina Society, Santa Fe, NM: Photodynamic Therapy of Choroidal Neovascularization Using Liposomal Benzoporphyrin Derivative Mono-acid (BPD-MA) (Speaker)
- 1995 International Symposium of Experimental and Clinical Ocular Pharmacology and Pharmaceuticals, Geneva, Switzerland: Photodynamic Therapy (Moderator and Speaker)
- 1995 Invited Speaker, Boston Veterans Administration Hospital: Developments in Macular Degeneration
- 1996 Invited Speaker, ARVO: Mini symposium: Current Understanding of Macular Degeneration
- 1996 ARVO: Selected Angiographic Findings Following Photodynamic Therapy of Choroidal Neovascularization (Speaker)
- 1996 Invited Speaker, Gordon Conference. Photodynamic Therapy
- 1996 Invited Speaker and Moderator, Macular Workshop, Bath, England. Ocular Neovascularization
- 1996 Club Jules Gonin, Bern, Switzerland. Photodynamic Therapy; Speaker
- 1996 Invited Speaker, American Academy of Ophthalmology, Subspecialty Day Symposium. New Developments in Age-Related Macular Degeneration
- 1996 Invited Speaker, Boston University School of Medicine. Retina Conference. Posterior Segment Complications of Cataract Surgery
- 1997 Invited Speaker, Cleveland Clinic Ophthalmology Conference, VEGF and Ocular Neovascularization
- 1997 Invited Speaker, Pan Hellenic Congress, Athens, Greece. VEGF and Ocular Neovascularization

- 1997 Invited Speaker and Moderator, International Symposium of Experimental and Clinical Ocular Pharmacology and Pharmaceutics, Munich, Germany. Photodynamic Therapy
- 1997 Invited Speaker, IBC's Conference on Ocular Disorders. Novel Therapeutic Development for Neovascular Diseases of the Eye, Boston, MA
- 1997 Invited Speaker, Research to Prevent Blindness Science Writer's Seminar, Los Angeles, CA
- 1997 Invited Panelist and Luncheon Discussant, American Academy of Ophthalmology Subspecialty Day Symposium, Update on Age-related macular degeneration and Photodynamic Therapy, San Francisco, CA
- 1997 Invited Speaker, Macula Society Symposium, American Academy of Ophthalmology, Other Experimental Treatment Modalities, San Francisco, CA
- 1998 Speaker, Macula Society, Expression of VEGF in Experimental Choroidal Neovascularization, Boca Raton, FL
- 1998 Invited Speaker, Aspen Retina Society, VEGF and Neovascularization, and Photodynamic Therapy for AMD, Aspen, CO
- 1998 Speaker, ARVO: Comparison of fluorescein angiography and indocyanine green angiography after photodynamic therapy for choroidal neovascularization
- 1998 Visiting Professor, University of Cincinnati, VEGF and Neovascularization, Photodynamic Therapy, and Alternative Treatments of AMD, Cincinnati, OH
- 1998 Invited Speaker, Pathogenesis and Treatment of Age-Related Macular Degeneration, Wilmer Ophthalmological Institute, Baltimore, MD
- 1998 Invited Speaker, The Albany Medical College: VEGF and Ocular Neovascularization; Photodynamic Therapy for AMD, Albany, NY
- 1998 Invited Speaker, New England Chapter Ophthalmic Photographers Society: Interpretation of ICG Angiography
- 1998 Speaker, Club Jules Gonin, Update on Clinical Trials of PDT for AMD, Edinburgh, Scotland
- 1998 Speaker, The Retina Society, Integrin Expression in Experimental Choroidal Neovascularization, Washington, DC
- 1998 Speaker, IIIe Symposium International de Creteil, Rationale of PDT for AMD, Paris, France
- 1998 Visiting Professor, University of North Carolina, Chapel Hill, NC, PDT for AMD and the Role of VEGF in Ocular Neovascularization
- 1999 Invited Speaker, Rhode Island Hospital, Providence, RI, PDT for AMD and the Role of VEGF in Ocular Neovascularization
- 1999 Invited Speaker, Schepens Eye Research Institute, Boston, MA, PDT for AMD
- 1999 Rosenthal Award Presentation, Macula Society, San Diego, CA, New Treatments for AMD
- 1999 Invited Speaker, Ninth National Masters Club Meeting, Tarpon Springs, FL, PDT for AMD and Pharmacologic Treatment for AMD

- 1999 Invited Speaker, 29<sup>th</sup> Anniversary Meeting of the Wilmer Retinal Vascular Center, Baltimore, MD, The Rationale of Photodynamic Therapy
- 1999 Invited Speaker, Oxford Ophthalmological Congress, Oxford, England, Retinal Vascular Dysfunction
- 1999 Invited Speaker, Research to Prevent Blindness Science Writer's Seminar, Los Angeles, CA
- 1999 Invited Speaker, American Academy of Ophthalmology, Subspecialty Day Symposium, Orlando, FL, Rationale of Photodynamic Therapy
- 1999 Speaker, The Retina Society, Photodynamic Therapy of Experimental CNV Using Lutetium Texaphyrin, Hawaii
- 2000 Invited Speaker and Moderator, International Symposium of Experimental and Clinical Ocular Pharmacology and Pharmaceutics, Lisbon, Portugal. Photodynamic Therapy.
- 2000 Invited Speaker, Wills Retina Service 40<sup>th</sup> Anniversary, Anti-angiogenesis and Growth Factors; Photodynamic Therapy, Philadelphia, PA
- 2000 Invited Speaker, Vale Vitrectomy Meeting, Photodynamic Therapy, Vale, CO
- 2000 Invited Speaker, International Conference on Photodynamic Therapy, Lausanne, Switzerland
- 2000 Invited Speaker, Minisymposium on Photodynamic Therapy, Association for Research in Vision and Ophthalmology, Ft. Lauderdale, FL
- 2000 Invited Speaker, Symposium on Retinal Disease, Vitreoretinal Complications of Cataract Surgery. American Society of Cataract and Refractive Surgery, Boston, MA
- 2000 Invited Speaker, New England Ophthalmological Society, Photodynamic Therapy, Clinical Indications and Treatment
- 2000 Invited Speaker, Canadian Retina Society, Photodynamic Therapy for Macular Degeneration, Whistler, British Columbia
- 2000 Invited Speaker, Canadian Ophthalmological Society, New Treatments for Macular Degeneration, Whistler, British Columbia
- 2000 Invited Speaker, Vision Quest 2000: 11<sup>th</sup> World Congress of Retina International, Toronto, Ontario, Canada
- 2000 Speaker, Club Jules Gonin, One-Year Results of the Verteporfin in Photodynamic Therapy (VIP) Study for AMD, Taormina, Sicily
- 2000 Invited Speaker, China National Ophthalmic Society, Photodynamic Therapy for Macular Degeneration, Shanghai, China
- 2000 Invited Speaker, International Conference on Eye Research, Anti-VEGF Therapy, Santa Fe, NM
- 2000 Invited Speaker, Vitreo-retinal Subspecialty Day, American Academy of Ophthalmology, One-Year Results of the Verteporfin in Photodynamic Therapy (VIP) Study for Pathologic Myopia, Dallas, TX
- 2000 Invited Speaker, Albert E. Sloane, Eye Forum, Advances in Macular Degeneration, Boston, MA

2000 Invited Speaker, New England Ophthalmological Society, Update on Photodynamic Therapy and Practical Issues for Nurses, Boston, MA

2000 Invited Speaker, New England Ophthalmological Society, Photodynamic Therapy, Clinical Indications and Treatment

2001 Visiting Professor, Universite Laval, Update on Photodynamic Therapy, Quebec City, Canada

2001 Invited Speaker, Aspen Retinal Detachment Society, Update on Photodynamic Therapy and Anti-angiogenic Therapy for Macular Degeneration, Aspen, CO

2001 Visiting Professor, University of Alberta, New Treatments for Macular Degeneration, Edmonton, Alberta, Canada

2001 Invited Speaker, Yale University Alumni Day, Photodynamic Therapy and Anti-angiogenic Therapy for Neovascular Macular Degeneration

2001 Breakout Session Leader for the Special Senses, Health Care, East and West, Moving into the 20<sup>th</sup> Century, Boston, MA

2001 Invited Speaker, Kevin Hill Course, Photodynamic therapy, Waterville, ME

2001 Visiting Professor, Photodynamic Therapy and the Development of Pharmacologic Therapy for AMD and PDR, Washington University, St. Louis, MO

2001 Invited Speaker, Second Symposium on Aging Retina and Early Degeneration, Schepens Eye Research Institute, Boston, MA

2001 Invited Speaker, Vitreo-retinal Subspecialty Day, American Academy of Ophthalmology, Other Photosensitizers for Photodynamic Therapy, New Orleans, LO

2002 Invited Speaker, Experimental Animal Models of Choroidal Neovascularization. Association for Research in Vision and Ophthalmology Annual Meeting, Ft. Lauderdale, FL

2002 Invited Speaker, Pharmacological Inhibition of Retinal and Choroidal Neovascularization: New Strategies and Future Frontiers. Association for Research in Vision and Ophthalmology Annual Meeting, Ft. Lauderdale, FL

2002 Invited Speaker, Drug Delivery to the Posterior Segment. Joint Clinical Research Center, Schepens Eye Research Institute and the Massachusetts Eye and Ear Infirmary

2002 Speaker, Macula Society Annual Meeting, Combined rhuFab V2 and Visudyne Therapy, Barcelona, Spain

2002 Jules Gonin Lecture, Club Jules Gonin: The Development of PDT for AMD. Montreux, Switzerland

2002 Speaker, Combined Meeting of the Retina and Vitreous Society, Targeted Photodynamic Therapy using a Homing Peptide to VEGFR2, San Francisco, CA

2002 Invited Speaker, Vitreo-retinal Subspecialty Day, American Academy of Ophthalmology, Expanding Indications for PDT in AMD, Orlando, FL

2002 Invited Speaker, University of San Francisco Department of Ophthalmology, Ophthalmology 2003; Update on Photodynamic

- Therapy and New Treatments for Retinal Diseases, San Francisco, CA
- 2003 Invited Speaker, Biannual Alcon Research Institute Meeting, Photodynamic Therapy for Choroidal Neovascularization, Fr. Worth, TX
- 2003 Invited Speaker, Schepens Eye Research Institute, Harvard Medical School, Photodynamic Therapy for Choroidal Neovascularization, Boston, MA
- 2003 Invited Speaker, Wellman Laboratories of Photomedicine, Lester Wolfe Workshop in Laser Biomedicine. Neovascularization in the Eye
- 2003 Speaker, Retina Society, Combined Angiostatin and Verteporfin PDT for the Treatment of Experimental Choroidal Neovascularization in the Rat, Chicago, IL
- 2003 Visiting Professor, Cole Eye Institute, New Therapies for Age related Macular Degeneration, Cleveland, OH
- 2003 Named Lecture; The First Annual Robert Haimovici, MD Lecture, Treating Choroidal Neovascularization: Beyond PDT, Boston University School of Medicine, Boston, MA
- 2003 Panel Discussant, American Academy of Ophthalmology Subspecialty Day, Controversies in AMD
- 2003 Named Lecture; Walter Wright Speaker, University of Toronto School of Medicine, New Treatments for AMD, Toronto, Ont.
- 2004 Speaker, Macula Society Annual Meeting, Search for Genes Expressed in Leukocytes that may serve as biomarkers for Neovascular Age-related Macular Degeneration, Las Vegas, NV
- 2004 Invited Speaker, New England Ophthalmologic Society, PDT, Anti-VEGF and the Alphabet Soup of Drug Therapy of AMD, Boston, MA
- 2004 Moderator, Association for Research in Vision and Ophthalmology, Experimental Choroidal Neovascularization, Ft. Lauderdale, FL
- 2004 Invited Speaker, 2004 Wisconsin EYEMD Spring Symposium. Alice McPherson Lecture, New Technologies for Age-related Macular Degeneration, Lake Geneva, WI
- 2004 Invited Speaker, Cornell Ophthalmology Alumni Association, Update on Age-related Macular Degeneration, New York, NY
- 2004 Panel Discussant, American Academy of Ophthalmology Subspecialty Day, Alternative, Pharmacologic, and Surgical Treatment of AMD
- 2004 Invited Speaker, American Academy of Ophthalmology Subspecialty Day, Pharmacotherapies: Now and in the Future
- 2005 Invited Speaker, Schepens Eye Research Institute, Treatment of AMD: Where do we go next?, Boston, MA
- 2005 Speaker and Moderator, Macula Society Annual Meeting, Potent Stable siRNA to Human VEGF for the Treatment of Ocular Neovascular Disease, Key Biscayne, FL
- 2005 Invited Speaker, Retina Summit, Epidemiology and Genetics of AMD, Cleveland, OH



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| 2005 | Speaker, American Society of Retina Surgeons, Randomized, Controlled Phase III Study of Ranibizumab (Lucentis™) for Minimally Classic or Occult Neovascular Age-related Macular Degeneration, Toronto, Ontario, Canada. |
| 2005 | Co-moderator, American Society of Retina Surgeons, Treatment of AMD, Toronto, Ontario, Canada.  |
| 2005 | Moderator, American Academy of Ophthalmology, Photodynamic Therapy: Verteporfin/Miravant, Chicago, IL   |
| 2005 | Speaker, American Academy of Ophthalmology, Intraocular Antagonism of VEGF for Treatment of CNV or DME, Chicago, IL   |

### **Leadership Roles**

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| 1991  | Laser Therapy of Ocular Disease (Speaker and Course Co-Director)   |
| 1991  | Greater Boston Lecture Series; Retina Section (Speaker and Course Co-Director)   |
| 1995  | Course Director Kevin Hill Ophthalmology Course. Update on Retinal Disease. Neovascular Disorders and Pediatric Retina. Organizer program, select and recruit speakers, edit syllabus, chair meeting |
| 1995  | International Symposium of Experimental and Clinical Ocular Pharmacology and pharmaceuticals, Geneva, Switzerland. Photodynamic Therapy (Moderator and Speaker)                                      |
| 1996  | Invited Speaker and Moderator, Macular Workshop, Bath, England. Ocular Neovascularization.   |
| 1997- | Advisory Board, International Symposium of Experimental and Clinical Ocular Pharmacology and Pharmaceuticals. Organize program, select and recruit speakers, edit syllabus, chair meeting            |

### **Report of Clinical Activities**

#### **Clinical Practice**

The clinical practice is medical and surgical diseases of the retina, with special emphasis on age-related macular degeneration. The practice site is the Retina Service of the Massachusetts Eye and Ear Infirmary, a teaching affiliate of Harvard Medical School. Clinical effort is approximately 50%, with time divided between office visits, outpatient lasers and surgery, with associated teaching of medical students, residents, and fellows. Patients are generally referred by ophthalmologists, and particularly in the case of macular degeneration patients, are referred from the New England region, nationally and internationally. The macular degeneration patients are frequently complicated consults from other retina specialists requiring special expertise in diagnosis and/or therapy.

#### **Clinical Contributions**

The major clinical contribution is the development of photodynamic therapy for neovascular macular degeneration, from pre-clinical studies through clinical trials, and receiving approval by health authorities in the United States and abroad. This represents a major innovation in the

treatment of neovascular macular degeneration, a common blinding disorder, with broader application to other forms of choroidal neovascularization, as well as iris and corneal neovascularization. The Rosenthal Award of the Macula Society and the Retina Research Award of the Club Jules Gonin were awarded for this work.

A second major clinical contribution is the identification of a particular growth factor, vascular endothelial growth factor (VEGF), as the major growth factor responsible for pathologic neovascular in ocular disorders including diabetic retinopathy and neovascular macular degeneration. Drugs targeting this growth factor are currently under clinical investigation in the US and Europe. The Alcon Research Institute Award was awarded for the work in PDT and VEGF.

### **Clinical Trials**

Principal Investigator in multi-center clinical trials of therapy for neovascular macular degeneration, including the Interferon Study Group, the Treatment of Age-related Macular Degeneration with Photodynamic Therapy Study, the Verteporfin in Photodynamic Therapy Study, Lu-Tex Photodynamic Therapy Study, and the rhuFab Therapy for Macular Degeneration Study.

### **Bibliography:**

#### **Original Reports**

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3. Miller JW, Stinson WG, Folkman J. Regression of experimental iris neovascularization with systemic alpha-interferon. Ophthalmology 1993; 100:9.
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19. Pharmacological Therapy for Macular Degeneration Study Group. Interferon Alfa-2a is Ineffective for Patients With Choroidal Neovascularization Secondary to Age-Related Macular Degeneration: Results of a Prospective Randomized Placebo-controlled Trial. *Arch Ophthalmol* 1997; 115: 865-872.

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## **Reviews, Chapters and Editorials**

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